

REMARKS

Applicant acknowledges with appreciation the Examiner's recognition that claim 2 recites allowable subject matter. Prior to entry of this Amendment, Claims 1-11 were
5 pending and under consideration. No Claims are being amended or cancelled. Claims 36-44 are newly added. Thus, after entry of this Amendment, claim 1-11 and 36-44 are pending.

Objection to the Oath or Declaration

10 The declaration was objected to because the country of citizenship was not indicated for one of the inventors and because a docket number was altered. A new declaration is being prepared and will be provided at a later date.

Amendment to the Claims

15 Claims 36-44 have been newly added. New Claims 36-44 are identical to originally filed Claims 3-11, with the exception that they ultimately depend from Claim 2, which recites allowable subject matter. Basis for these claims can be found throughout the application as originally filed, for example in the originally filed Claims. No new matter is added by this amendment.

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The Amendments of the Specification

The specification has been amended to correct the wording of the priority claims. Basis for this amendment is found at page 1, line 3 of the application, on the Patent Application Transmittal form filed July 30, 2001 and in the declaration filed January 8,
25 2002.

The specification has also been amended to include references to Figures 3C-1, 3C-2, 4A and 4B. Basis for this amendment is found in the drawings as originally filed. This amendment does not introduce new matter.

Objections to the Specification

The specification was objected to for inappropriate references to the figures filed with the preliminary amendment filed November 19, 2001. The specification has now been amended to include references to all of these figures, thus obviating the objection.

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Rejection of Claims 1 and 6-8 Under 35 U.S.C. §102(b)

Claims 1 and 6-8 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Norden *et al.*, 1988, J. Biol. Chem. 273:15682-15686 (Norden *et al.*). Applicant traverses the rejection.

10 To anticipate a claim under 35 U.S.C. § 102(b), a reference must teach every element of the rejected claim (MPEP § 2131).

The Norden *et al.* reference neither teaches nor suggests every element of the rejected claims. Specifically, Norden *et al.* do not teach an analog probe. The Patent Office has stated that "...the free poly (dεA) is an analog probe..."(see second paragraph
15 on Page 5 of Office Action). However, an analog probe is defined in the specification as "a nucleic acid containing modification to the naturally-occurring phosphodiester linkages or modification to the naturally-occurring ribose backbone" (page 13, lines 30-31). The structure of poly(1,N⁶-etheno-deoxyadenosine) (dεA) includes a modified base (a modified adenosine) but clearly does *not* contain a modified phosphodiester linkage or a
20 modification to the ribose backbone. 1,N⁶-ethenoadenine is an analog of adenine. The structure of 1,N⁶-ethenoadenine (available from Sigma as product No. E4007) is provided herein as Exhibit A. Thus, poly(1,N⁶-etheno-deoxyadenosine) is a DNA having 1,N⁶-ethenoadenine residues at the 1 position of the deoxyribose ring.

Accordingly, since the cited reference fails to teach each and every limitation of the
25 rejected Claims, Applicants request that the rejection of Claims 1 and 6-8 under 35 U.S.C. § 102(b) be withdrawn.

Rejection of Claims 1 and 3-8 Under 35 U.S.C. §103(a)

Claims 1 and 3-8 stand rejected under 35 U.S.C. § 103(a) as allegedly being
30 unpatentably obvious over Norden *et al.* in view of Faruqi *et al.*, 1998, Proc. Natl. Acad. Sci. US 95:1394-1403 (Faruqi *et al.*). Applicants traverse the rejection.

In rejecting claims under §103(a), the Patent Office bears the burden of establishing a *prima facie* case of obviousness (MPEP § 2142). To establish a *prima facie* case, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine their teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference(s) must teach or suggest each and every limitation of the rejected claims. The teaching or suggestion to make the claimed combination *and* the reasonable expectation of success must *both* be found in the prior art, and *not* in Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP §2142.

Norden *et al.* teach a RecA coated poly(dεA), but do not teach or suggest an analog probe, as discussed above.

Faruqi *et al.* teach a peptide nucleic acid (PNA) that can bind to single stranded DNA and to form triple helices. Faruqi *et al.* do not teach or suggest the use of RecA.

The Patent Office states that according to Norden *et al.*, and further in view of Faruqi *et al.*, it would have been obvious to have made a composition comprising an analog probe (e.g. PNA) and a first single stranded nucleic acid probe that is coated with a recombinase (e.g. RecA) as recited in Claim 1. Applicants disagree.

There is no motivation in the references to combine them as indicated by the Patent Office.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggest the desirability of the combination. (MPEP § 2143.01 citing *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)). The Patent Office has presented no motivation to combine the Norden *et al.* and the Faruqi *et al.* references.

The Patent Office has stated that it would be “prima facie obvious to one having ordinary skill in the art at the time the invention was made because the replacement of oligo (dT) in RecA-poly(A)-oligo(dT) complex taught by Faruqi *et al.*, by its corresponding PNA would generate a more stable nucleic acid hybrid.”¹ However, if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, *then there is no suggestion or motivation to make the proposed*

modification. (MPEP § 2143.01 citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)).

5 The purpose of the Norden *et al.* reference is to determine the nucleobase orientation of the first and the second bound DNA strands in a RecA DNA filament. As mentioned above, the Patent Office stated that one would be motivated to add PNA to the RecA DNA filament. However, upon addition, PNA might bind to one of these filaments due to its high affinity. This binding by PNA would likely disrupt the filament structure, and would interfere with the ability to determine base orientation, thus frustrating the purpose of Norden *et al.* to determine the filament structure.. The modification of Norden
10 *et al.* reference by the addition of PNA would render the methods of Norden *et al.* unsatisfactory for its intended purpose. Therefore, there is no motivation to add PNA to the RecA DNA filaments of Norden *et al.*

 Faruqi *et al.* teaches that one can add PNA to single stranded DNA to form a stable structure, and further teach that PNA can be introduced into cells to direct mutations at a
15 target site in chromosomal DNA. There is no teaching or suggestion of using RecA in Faruqi *et al.* If one were to add RecA to a PNA and attempt to introduce that combination into cells, the result would be completely unpredictable, and there is no reasonable expectation that anything useful or advantageous would result.

 Therefore, there is no motivation in Norden *et al.* to use PNA, and there is no
20 motivation in Faruqi *et al.* to use RecA.

 The attempt to use the prior art in a mosaic fashion by the Patent Office, using the Applicants' disclosure as a template and selecting only those teachings that are necessary to support a rejection while ignoring their context and/or other teachings in the same document, constitutes a legally improper "hindsight" reconstruction:

25 It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.

In re Gorman, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991); *see also, Interconnect Planning Corp.*, 227 USPQ 543, 551 (Fed. Cir. 1985) ("When prior art references require selective
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combination to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight obtained from the invention itself.”).

5 The Patent Office also alleged that “the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected function to achieve their expected results when combined for their common known purpose.” However, the achievement of expected results in this instance (i.e. binding of PNA to the RecA filament) cannot provide motivation, since as indicated above, the proposed substitution of a PNA for one of the strands in the RecA filament would give an unpredictable result or would render the Norden *et al.* reference unsatisfactory for its intended purpose.

10 The Patent Office has alleged that “there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results.” However, the combination of elements in Claim 1, and claims depending therefrom, do give an unobvious or unexpected result. The combination of PNA with single stranded nucleic acids probes improves the efficiency of polynucleotide targeting by recombinase coated single stranded nucleic acid probes. The case (*In re Rose* 220 F.2d 459, 105 USPQ 237 (CCPA 1955)) cited by the Patent Office concerns claims to an apparatus and methods for packaging, handling and storing lumber, a mechanical invention having conventional and predictable elements. This is in stark contrast to the instant claims and invention, which deal with biochemical compounds having unpredictable properties, and which Applicant has discovered to give unexpected results.

20 Accordingly, Applicants request that the rejection of Claims 1 and 3-8 under 35 U.S.C. § 103(a) be withdrawn.

25 Newly added Claim 36-44 ultimately depend from Claim 2, which the Patent Office indicated as reciting allowable subject matter. As a consequence, Claims 36-44 likewise recite allowable subject matter.

Conclusion

30 Applicants submit that amended Claims 1-44 satisfy all of the statutory requirements for patentability and are in condition for allowance. An early notification of

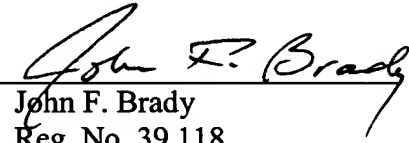
the same is kindly solicited.

No fees beyond those being submitted concurrently with this Amendment are believed due. However, the Commissioner is authorized to charge any required fee, or credit any overpayment, to Dorsey & Whitney LLP Deposit Account No. 50-2319 (Order
5 No. A-69625-1/AMP/JFB).

Respectfully submitted,

DORSEY & WHITNEY LLP

Date: October 23, 2003

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Serial No. 09/557,423